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NOGUEROLA, ALEXANDER STEPHAN	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/527,389	AUERSWALD ET AL.	
	Examiner	Art Unit	
	ALEX NOGUEROLA	1795	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03/10/2005 (preliminary amendment)*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 March 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *03/10/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

2. Claims 1, 2, 5, 7-9, 14, and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Pethig et al. WO 97/34689 A1 ("Pethig").

Addressing claim 1, Pethig discloses a fluidic system for analysing biomolecules comprising an inlet port ("Inlet 2" – Figure 1), an outlet port ("Outlet 1" or "Outlet 2" or "Waste"), a set of microelectrodes ("Trap 2" and page 10, lines 22 – page 11, line 09)

within a channel connecting the inlet and outlet ports (Fig. 1), means for flowing a fluid through the fluidic system (implied by page 07, lines 05-07, which discloses feeding a sample into Inlet 2, and also implied by arrows shown in Figure 1, which indicate flowing fluid), means for flowing a suspension of a given type of microparticles through the fluidic system (implied by page 07, lines 05-07, which discloses feeding a sample into Inlet 2, and also implied by arrows shown in Figure 1, which indicate flowing fluid), means for applying an AC voltage having an appropriate frequency for retaining a given type of microparticles in the region of the electrodes by means of positive (attractive) dielectrophoresis (implied by page 07, lines 09-10, which states “Trap T2 is of a selective nature and, at this time configured to trap the latex beads.”), the microparticles being functionalized with appropriate ligand molecules (page 07, lines 05-07), and means for flowing a sample fluid containing the analyte specifically bound by the ligand molecules on the microparticles through the fluidic system, thereby perfusing the retained microparticles (page 07, lines 22-27, which discloses releasing all trapped particles, including microparticles with analyte bound thereon, and flowing them towards junction JC).

Addressing claim 2, the claimed means for flowing a plurality of types of particles and means for applying different frequency voltages are implicitly disclosed by such passages in Pethig as cited in the rejection of claim 1 that teach feeding a sample flow into inlet 2 and retaking microparticles using an appropriate frequency, and by

"In the apparatus of the present invention, the channels may be wider, so as to permit controlled manipulation of many particles at the same time. [emphasis added]" (page 03, lines 28-30);

"… many of the types of apparatus within the scope of the present invention may be thought of as made up of a set of modules or components, each designed to do a particular task such as concentrating particles together, separating one type of particle from another, trapping particles of a particular type and subjecting particles to bulk movement.[emphasis added]" (page 04, lines 03-09); and

page 11, line 24 – page 12, line 13, which discloses applying a particular frequency voltage to trap certain non-viable cells and applying another particular frequency voltage to trap viable cells.

In sum, the apparatus of Pethig is clearly configured to flow a mixture of microparticles and substances therein and selectively retain micropartcles or other substances from the mixture by applying an appropriate frequency to trapping electrodes.

Addressing claim 5, barring a contrary showing, according to the Examiner's understating of the specification the means for flowing a solution containing reagent molecules specific to the analyte molecules through the fluidic system to perfuse the analyte bound by the ligand molecules on the microparticles can be the same as the means for flowing a suspension of a given type of microparticles through the fluidic system in claim 1 or the means for flowing a fluid through the fluidic system in claim 1.

Addressing claim 7, for the additional limitation of this claim see, for example, page 07, lines 17-20, which states, "Non-microorganism particles experience a traveling field which will move them out of Trap T2 and along conveyor track Z to a waste outlet 8."

Addressing claim 8, for the additional limitations of this claim see page 07, line 13 – page 08, line 08.7

Addressing claim 14, since Pethig discloses means for dielectrophoretically trapping the microparticles and releasing them at will Pethig implicitly discloses means for trapping the and releasing them at will and thus as claimed, if so desired. See page 07, lines 01-27.

Addressing claim 15, for the additional limitations of this claim see Figure 2; page 07, lines01-05; and page 09, 25 – page 10, line 21.

3. Claims 1, 2, 4, 5, 7, 14, and 15 are rejected under 35 U.S.C. 102(e) as being anticipated by Gomez et al. US 7,306,924 B2 ('Gomez").

Addressing claim 1, Gomez discloses a fluidic system for analysing biomolecules comprising an inlet port (28 – Figure 1), an outlet port (30), a set of microelectrodes (36) within a channel connecting the inlet and outlet ports (Fig. 1), means for flowing a fluid through the fluidic system (implied by the arrows shown at the inlet port and outlet port. Also see col. 17:50-53 and claim 11, line 3), means for flowing a suspension of a given type of microparticles through the fluidic system (implied by the arrows shown at the inlet port and outlet port. Also see col. 17:50-53 and claim 11, line 3), means for applying an AC voltage having an appropriate frequency for retaining a given type of microparticles in the region of the electrodes by means of positive (attractive) dielectrophoresis (col. 32:11-15 and col. 31:38-41), the microparticles (128) being functionalized with appropriate ligand molecules (col. 32:11 and col. 31:35-37), and

means for flowing a sample fluid containing the analyte specifically bound by the ligand molecules on the microparticles through the fluidic system (col. 32:16-21), thereby perfusing the retained microparticles (col. 32:16-21).

Addressing claim 2, as discussed in the rejection of claim 1 Gomez discloses "means for flowing a suspension of a given type of microparticles through the fluidic system (implied by the arrows shown at the inlet port and outlet port. Also see col. 17:50-53 and claim 11, line 3), means for applying an AC voltage having an appropriate frequency for retaining a given type of microparticles in the region of the electrodes by means of positive (attractive) dielectrophoresis (col. 32:11-15 and col. 31:38-41)." Additionally, Gomez states, "The frequency and magnitude of an alternating electric field **158** produced by the electrodes **156**, together with the conductivity of the carrier medium, are chosen so that the microorganisms **160** of interest are retained inside the chamber **154** by the DEP force (in the same way as beads **128** were retained in the previous capture method). [emphasis added]" See col. 32:36-42. The apparatus of Gomez is thus clearly configured with means to flow a mixture of microparticles and substances therein and means to selectively retain microparticles or other substances from the mixture by applying an appropriate frequency to trapping electrodes.

Addressing claim 4, the claimed means for detecting the presence of the analyte bound to the micro particles at the retention site of the microparticles is implied in Gomez because the cavities containing the retention sites as detection/collection chambers. See col. 32:11-15. Also see co. 30:31-56.

Addressing claim 5, barring a contrary showing, according to the Examiner's understating of the specification the means for flowing a solution containing reagent molecules specific to the analyte molecules through the fluidic system to perfuse the analyte bound by the ligand molecules on the microparticles can be the same as the means for flowing a suspension of a given type of microparticles through the fluidic system in claim 1 or the means for flowing a fluid through the fluidic system in claim 1.

Addressing claim 7, for the additional limitation of this claim see col. 32:21-27.

Addressing claim 8, for the additional limitation of this claim note that Gomez states, "Alternatively, a separate set of electrodes, preferably with interdigitated finger parts may be provided for measurement purposes." See col. 07:35-39.

Addressing claim 9, for the additional limitations of this claim see Figures 1-4; col. 07:25-35; and col. 13:50 – col. 15:67

Addressing claim 14, since Gomez discloses means for dielectrophoretically trapping the microparticles and releasing them at will Pethig implicitly discloses means for trapping the and releasing them at will and thus as claimed, if so desired. See page 07, lines 01-27.

Addressing claim 15, for the additional limitations of this claim see col. 28:40-44.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 3, 4, 6, 9, and 16-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pethig et al. WO 97/34689 A1 ("Pethig").

Addressing claim 3, Pethig discloses a fluidic system for analysing biomolecules comprising an inlet port ("Inlet 2" – Figure 1), an outlet port ("Outlet 1" or "Outlet 2" or "Waste"), a set of microelectrodes ("Trap 2" and page 10, lines 22 – page 11, line 09) within a channel connecting the inlet and outlet ports (Fig. 1), means for flowing a fluid through the fluidic system (implied by page 07, lines 05-07, which discloses feeding a sample into Inlet 2, and also implied by arrows shown in Figure 1, which indicate flowing fluid), means for flowing a suspension of a given type of microparticles through the fluidic system (implied by page 07, lines 05-07, which discloses feeding a sample into Inlet 2, and also implied by arrows shown in Figure 1, which indicate flowing fluid), means for applying an AC voltage having an appropriate frequency for retaining a given type of microparticles in the region of the electrodes by means of positive (attractive) dielectrophoresis (implied by page 07, lines 09-10, which states "Trap T2 is of a selective nature and, at this time configured to trap the latex beads."), the microparticles being functionalized with appropriate ligand molecules (page 07, lines 05-07), and means for flowing a sample fluid containing the analyte specifically bound by the ligand molecules on the microparticles through the fluidic system, thereby perfusing the retained microparticles (page 07, lines 22-27, which discloses releasing all trapped particles, including microparticles with analyte bound thereon, and flowing them towards junction JC).

Additionally, the claimed means for flowing a plurality of types of particles and means for applying different frequency voltages are implicitly disclosed by such passages in Pethig as cited above that teach feeding a sample flow into inlet 2 and retaking microparticles using an appropriate frequency, and by

"In the apparatus of the present invention, the channels may be wider, so as to permit controlled manipulation of many particles at the same time. [emphasis added]" (page 03, lines 28-30);

"… many of the types of apparatus within the scope of the present invention may be thought of as made up of a set of modules or components, each designed to do a particular task such as concentrating particles together, separating one type of particle from another, trapping particles of a particular type and subjecting particles to bulk movement.[emphasis added]" (page 04, lines 03-09); and

page 11, line 24 – page 12, line 13, which discloses applying a particular frequency voltage to trap certain non-viable cells and applying another particular frequency voltage to trap viable cells.

In sum, the apparatus of Pethig is clearly configured to flow a mixture of microparticles and substances therein and selectively retain microparticles or other substances from the mixture by applying an appropriate frequency to trapping electrodes.

As for providing a plurality of sets of microelectrodes within the channel at spaced intervals, and means for applying voltages of selected frequencies to each of the sets of electrodes to retain selected types of microparticles at the electrodes these

features are obvious over Pethig. Providing a plurality of sets of microelectrodes is just multiplication of parts for a multiplied effect (the ability to retain multiple microparticles in different regions of the device), which is *per se* obvious. See MPEP 2144.04.VI.B. Moreover, Pethig shows in Figure 1 two dielectrophoresis traps, albeit not in the same channel, for trapping different micropartcles or substances. See also page 06, line 31 – page 07, line 15. Pethig also states, "… many of the types of apparatus within the scope of the present invention may be though of as made up of a set of modules or components, each designed to do a particular task such as concentrating particles together, separating one type of particle from another, trapping particles of a particular type and subjecting particles to bulk movement. [emphasis added]" See page 04, lines 01-09. Thus, even if multiplication of parts for a multiplied effect was not *per se* obvious in light of Pethig alone providing a plurality of sets of microelectrodes within the channel is obvious.

Addressing claim 4, Pethig discloses a fluidic system for analysing biomolecules comprising an inlet port ("Inlet 2" – Figure 1), an outlet port ("Outlet 1" or "Outlet 2" or "Waste"), a set of microelectrodes ("Trap 2" and page 10, lines 22 – page 11, line 09) within a channel connecting the inlet and outlet ports (Fig. 1), means for flowing a fluid through the fluidic system (implied by page 07, lines 05-07, which discloses feeding a sample into Inlet 2, and also implied by arrows shown in Figure 1, which indicate

flowing fluid), means for flowing a suspension of a given type of microparticles through the fluidic system (implied by page 07, lines 05-07, which discloses feeding a sample into Inlet 2, and also implied by arrows shown in Figure 1, which indicate flowing fluid), means for applying an AC voltage having an appropriate frequency for retaining a given type of microparticles in the region of the electrodes by means of positive (attractive) dielectrophoresis (implied by page 07, lines 09-10, which states "Trap T2 is of a selective nature and, at this time configured to trap the latex beads."), the microparticles being functionalized with appropriate ligand molecules (page 07, lines 05-07), and means for flowing a sample fluid containing the analyte specifically bound by the ligand molecules on the microparticles through the fluidic system, thereby perfusing the retained microparticles (page 07, lines 22-27, which discloses releasing all trapped particles, including microparticles with analyte bound thereon, and flowing them towards junction JC).

Pethig does not mention providing means for detecting the presence of the analyte bound to the microparticles at the retention site of the microparticles. However, Pethig does disclose providing means for detecting the presence of the analyte bound to the microparticles at sites downstream from the microparticles. See for example, page 13, lines 29 – page 14, line 1. it would have been obvious to also provide means for detecting the presence of the analyte bound to the microparticles at the retention site of the microparticles similar to those provided downstream because (1) it would allow the operator to confirm that microparticles of interest have been retained at the retention site as desired before proceeding with releasing them for further processing, (2) this

detection means can be easily implemented as in the simplest embodiment it just requires a transparent cover and good eyesight, and (3) it would allow the operator to easily calibrate the electrode sets, that is to determine the appropriate frequencies for retaining different microparticles or microparticle-analyte complexes.

Addressing claim 6, Pethig discloses a fluidic system for analysing biomolecules comprising an inlet port ("Inlet 2" – Figure 1), an outlet port ("Outlet 1" or "Outlet 2" or "Waste"), a set of microelectrodes ("Trap 2" and page 10, lines 22 – page 11, line 09) within a channel connecting the inlet and outlet ports (Fig. 1), means for flowing a fluid through the fluidic system (implied by page 07, lines 05-07, which discloses feeding a sample into Inlet 2, and also implied by arrows shown in Figure 1, which indicate flowing fluid), means for flowing a suspension of a given type of microparticles through the fluidic system (implied by page 07, lines 05-07, which discloses feeding a sample into Inlet 2, and also implied by arrows shown in Figure 1, which indicate flowing fluid), means for applying an AC voltage having an appropriate frequency for retaining a given type of microparticles in the region of the electrodes by means of positive (attractive) dielectrophoresis (implied by page 07, lines 09-10, which states "Trap T2 is of a selective nature and, at this time configured to trap the latex beads."), the microparticles

being functionalized with appropriate ligand molecules (page 07, lines 05-07), and means for flowing a sample fluid containing the analyte specifically bound by the ligand molecules on the microparticles through the fluidic system, thereby perfusing the retained microparticles (page 07, lines 22-27, which discloses releasing all trapped particles, including microparticles with analyte bound thereon, and flowing them towards junction JC).

Barring a contrary showing, according to the Examiner's understating of the specification the means for flowing a solution containing reagent molecules specific to the analyte molecules through the fluidic system to perfuse the analyte bound by the ligand molecules on the microparticles can be the same as the means for flowing a suspension of a given type of microparticles through the fluidic system in claim 1 or the means for flowing a fluid through the fluidic system in claim 1.

Pethig does not mention detecting the presence of the reagent molecules bound to the microparticles at the retention site of the microparticles. As a first matter this claim only seems to add an intended use of the system, not an actual structural feature. In any event, Pethig does disclose providing means for detecting the presence of the analyte bound to the microparticles at sites downstream from the microparticles. See for example, page 13, lines 29 – page 14, line 1. It would have been obvious to also provide means for detecting the presence of reagent molecules bound to the microparticles at the retention site of the microparticles similar to those provided downstream because (1) it would allow the operator to confirm that microparticle-analyte complexes of interest (which may be been altered by reagent) have been

retained at the retention site as desired before proceeding with releasing them for further processing, (2) this detection means can be easily implemented as in the simplest embodiment it just requires a transparent cover and good eyesight, and (3) it would allow the operator to easily calibrate the electrode sets, that is to determine the appropriate frequencies for retaining different microparticles or micropaticle-anayte complexes. The use of the reagent may be for making the microparticle-analyte complex detectable by the detection means. For example, if visual detection is to be used the regent may be a colored chemical, such as a dye.

Addressing claim 9, Pethig discloses a fluidic system for analysing biomolecules comprising an inlet port ("Inlet 2" – Figure 1), an outlet port ("Outlet 1" or "Outlet 2" or "Waste"), a set of microelectrodes ("Trap 2" and page 10, lines 22 – page 11, line 09) within a channel connecting the inlet and outlet ports (Fig. 1), means for flowing a fluid through the fluidic system (implied by page 07, lines 05-07, which discloses feeding a sample into Inlet 2, and also implied by arrows shown in Figure 1, which indicate flowing fluid), means for flowing a suspension of a given type of microparticles through the fluidic system (implied by page 07, lines 05-07, which discloses feeding a sample into Inlet 2, and also implied by arrows shown in Figure 1, which indicate flowing fluid), means for applying an AC voltage having an appropriate frequency for retaining a given

type of microparticles in the region of the electrodes by means of positive (attractive) dielectrophoresis (implied by page 07, lines 09-10, which states “Trap T2 is of a selective nature and, at this time configured to trap the latex beads.”), the microparticles being functionalized with appropriate ligand molecules (page 07, lines 05-07), and means for flowing a sample fluid containing the analyte specifically bound by the ligand molecules on the microparticles through the fluidic system, thereby perfusing the retained microparticles (page 07, lines 22-27, which discloses releasing all trapped particles, including microparticles with analyte bound thereon, and flowing them towards junction JC).

Although Pethig does not specifically mention whether the fluidic system comprises a support with microstructured microelectrodes and structured microchannel(s), the support being of non-conducing material, such as glass or silicon, if not implied these features are strongly suggested by Pethig because Pethig discloses investigating reactions on a microscopic scale and making the fluidic system by photolithography and laser machining. See page, line 20 – page 03, line 30.

Addressing claim 16, Pethig discloses a method for analysis of biomolecules comprising the steps of:

a) providing a fluidic system having an inlet port ("Inlet 2" – Figure 1) and outlet port ("Outlet 1" or "Outlet 2" or 'Waste") and containing a set of microelectrodes ("Trap 2" and page 10, line 22 - page 11, line 09) and a means of moving fluid through the fluidic system (implied by page 07, lines 05-07, which discloses feeding a sample into inlet 2, and also implied by arrows shown in Figure 1, which indicate flowing fluid);

b) applying an AC voltage to the microelectrodes with an appropriate frequency for retaining in the region of the microelectrodes a given type of microparticles which are functionalized with appropriate ligand molecules by positive dielectrophoresis (since Pethig provides microelectrode means for retaining functional microbeads with antibodies, for example, to trap chemical or biochemical species of interest in a fluid flowed over the electrodes, this step is just using the microelectrodes are intended in at least one Pehtig embodiment - page 07, lines 01-17);

c) flowing a suspension of the type of microparticles through the fluidic system and retaining the microparticles at the microelectrodes by means of positive dielectrophoresis (again this step is just another aspect of how Pethig intends to use his apparatus - page 07, lines 01-17);

d) flowing a sample fluid containing the analyte specifically bound by the ligand molecules on the microparticles through the fluidic system, thereby perfusing the retaining microparticles (again this step is just another aspect of how Pethig intends to use his apparatus – abstract and associated figure and page 07, lines 01-17);

e) detecting the presence of analyte bound to the microparticles (page 07, line 31 – page 08, line 07).

Addressing claim 17, flowing a plurality of types of particles and applying different frequency voltages are implicitly disclosed by such passages in Pethig as cited in the rejection of claim 1 that teach feeding a sample flow into inlet 2 and retaking microparticles using an appropriate frequency, and by

"In the apparatus of the present invention, the channels may be wider, so as to permit controlled manipulation of many particles at the same time. [emphasis added]" (page 03, lines 28-30);

"… many of the types of apparatus within the scope of the present invention may be thought of as made up of a set of modules or components, each designed to do a particular task such as concentrating particles together, separating one type of particle from another, trapping particles of a particular type and subjecting particles to bulk movement.[emphasis added]" (page 04, lines 03-09); and

page 11, line 24 – page 12, line 13, which discloses applying a particular frequency voltage to trap certain non-viable cells and applying another particular frequency voltage to trap viable cells.

In sum, the apparatus of Pethig is clearly configured to flow a mixture of microparticles and substances therein and selectively retain micropartcles or other substances from the mixture by applying an appropriate frequency to trapping electrodes.

Addressing claim 18, Pethig does not mention providing means for detecting the presence of the analyte bound to the microparticles at the retention site of the microparticles. However, Pethig does disclose providing means for detecting the presence of the analyte bound to the microparticles at sites downstream from the microparticles. See for example, page 13, lines 29 – page 14, line 1. it would have been obvious to also provide means for detecting the presence of the analyte bound to the microparticles at the retention site of the microparticles similar to those provided downstream because (1) it would allow the operator to confirm that microparticles of interest have been retained at the retention site as desired before proceeding with releasing them for further processing, (2) this detection means can be easily implemented as in the simplest embodiment it just requires a transparent cover and good eyesight, and (3) it would allow the operator to easily calibrate the electrode sets, that is to determine the appropriate frequencies for retaining different microparticles or microparticle-analyte complexes.

Addressing claims 19, 20, and 22-24, barring a contrary showing, according to the Examiner's understating of the specification the means for flowing a solution containing reagent molecules specific to the analyte molecules through the fluidic system to perfuse the analyte bound by the ligand molecules on the microparticles can be the same as the means for flowing a suspension of a given type of microparticles through the fluidic system in claim 16 or the means for flowing a fluid through the fluidic system in claim 16.

Pethig does not mention detecting the presence of the reagent molecules bound to the microparticles at the retention site of the microparticles. Pethig does disclose providing means for detecting the presence of the analyte bound to the microparticles at sites downstream from the microparticles. See for example, page 13, lines 29 – page 14, line 1. It would have been obvious to also provide means for detecting the presence of reagent molecules bound to the microparticles at the retention site of the microparticles similar to those provided downstream because (1) it would allow the operator to confirm that microparticle-analyte complexes of interest (which may be been altered by reagent) have been retained at the retention site as desired before proceeding with releasing them for further processing, (2) this detection means can be easily implemented as in the simplest embodiment it just requires a transparent cover and good eyesight, and (3) it would allow the operator to easily calibrate the electrode sets, that is to determine the appropriate frequencies for retaining different microparticles or micropaticle-anayte complexes. The use of the reagent may be for

making the microparticle-analyte complex detectable by the detection means. For example, if visual detection is to be used the regent may be a colored chemical, such as a dye. Note that if the reagent is to enhance or enable detection of the analyte then when the reagent is detected the analyte, at least indirectly, will also be detected and vice verse. In any event, the apparatus of Pethig can clearly detect reagent or analyte as desired, since they are chemical or biochemical species. Also note that using a washing fluid and the sequence in which washing fluid and reagent is flowed is within the skill of one ordinary skill in the art at the time of the invention knowing the reaction involved between the reagent and analyte or microparticle to determine how to implement the reagent reaction and wash off excess reagent or unwanted chemical byproducts.

Addressing claim 21, for the additional limitation of this claim see, for example, page 07, lines 17-20, which states, “Non-microorganism particles experience a traveling field which will move them out of Trap T2 and along conveyor track Z to a waste outlet 8.”

Addressing claims 25-35, the additional limitations of these claims concern how long the AC field is applied, whether reagent is used and when during the analyte process, and whether, when rinsing is performed, and whether detection occurs in the regain region or outside of it. If not already taught by Pethig these steps are within the skill of one of ordinary sill in the art at the time of the invention as they are just optimizing the detection process. For example how long the microparticles are retained just depends on the whether the analyte-ligand reaction or analyte-reagent reactions have occurred to the extent desired (amount or volume of sample to evaluated and kinetics of the reactions) and whether detection will occur at the retaining site or not. Pethig does not mention detecting the presence of the reagent molecules bound to the microparticles at the retention site of the microparticles. Pethig does disclose providing means for detecting the presence of the analyte bound to the microparticles at sites downstream from the microparticles. See for example, page 13, lines 29 – page 14, line 1. It would have been obvious to also provide means for detecting the presence of reagent molecules bound to the microparticles at the retention site of the microparticles similar to those provided downstream because (1) it would allow the operator to confirm that microparticle-analyte complexes of interest (which may be been altered by reagent) have been retained at the retention site as desired before proceeding with releasing them for further processing, (2) this detection means can be easily implemented as in the simplest embodiment it just requires a transparent cover and good eyesight, and (3) it would allow the operator to easily calibrate the electrode sets, that is to determine the appropriate frequencies for retaining different microparticles or micropaticle-anayte

complexes. The use of the reagent may be for making the microparticle-analyte complex detectable by the detection means. For example, if visual detection is to be used the regent may be a colored chemical, such as a dye. Note that if the reagent is to enhance or enable detection of the analyte then when the reagent is detected the analyte, at least indirectly, will also be detected and vice verse. In any event, the apparatus of Pethig can clearly detect reagent or analyte as desired, since they are chemical or biochemical species. Also note that using a washing fluid and the sequence in which washing fluid and reagent is flowed is within the skill of one ordinary skill in the art at the time of the invention knowing the reaction involved between the reagent and analyte or microparticle to determine how to implement the reagent reaction and wash off excess reagent or unwanted chemical byproducts.

Addressing claim 36, Pethig discloses using conventional techniques for making the microfuidic system, such as photolithography or laser making. See page 3, the first and second full paragraphs. This would suggest to one with ordinary skill in the art at the time of the invention at least using a support made of glass or silicon.

Addressing claim 37, for the additional limitations of this claim see Figure 2;

page 07, lines01-05; and page 09, 25 – page 10, line 21.

Addressing claim 38, the relative size of the microelectrodes to the fluid channel width and the dimensions of the microelectrodes, such as width and gap spacing will just depend on the expected size of the microparticles, and the electrical field to be generated.

8. Claims 10 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pethig et al. WO 97/34689 A1 ("Pethig") in view of Van Ness US 5,994,065 ("Van Ness").

Addressing claim 10, Pethig discloses a fluidic system for analysing biomolecules comprising an inlet port ("Inlet 2" – Figure 1), an outlet port ("Outlet 1" or "Outlet 2" or "Waste"), a set of microelectrodes ("Trap 2" and page 10, lines 22 – page 11, line 09) within a channel connecting the inlet and outlet ports (Fig. 1), means for flowing a fluid through the fluidic system (implied by page 07, lines 05-07, which discloses feeding a sample into Inlet 2, and also implied by arrows shown in Figure 1, which indicate flowing fluid), means for flowing a suspension of a given type of microparticles through the fluidic system (implied by page 07, lines 05-07, which

discloses feeding a sample into Inlet 2, and also implied by arrows shown in Figure 1, which indicate flowing fluid), means for applying an AC voltage having an appropriate frequency for retaining a given type of microparticles in the region of the electrodes by means of positive (attractive) dielectrophoresis (implied by page 07, lines 09-10, which states "Trap T2 is of a selective nature and, at this time configured to trap the latex beads."), the microparticles being functionalized with appropriate ligand molecules (page 07, lines 05-07), and means for flowing a sample fluid containing the analyte specifically bound by the ligand molecules on the microparticles through the fluidic system, thereby perfusing the retained microparticles (page 07, lines 22-27, which discloses releasing all trapped particles, including microparticles with analyte bound thereon, and flowing them towards junction JC).

Pethig only appears to mention latex microbeads. See page 07, lines 5-7. However, this is only as an example. As shown by Van Ness polystyrene microbeads and latex microbeads were known alternative support material at the time of the invention so, barring a contrary showing, to substitute polystyrene microbeads for latex ,microbeads is just substitution of one known element for another with predictable results. The microbead composition and size would be chosen based factors such as the nature of the substances to be supported, how the supported substances are to be supported (chemical linking groups or adsorpotion), the amount of substance to be supported, and the ability of the electrical fields to retain large microbeads.

Addressing claim 39, Pethig discloses a method for analysis of biomolecules comprising the steps of:

a) providing a fluidic system having an inlet port ("Inlet 2" – Figure 1) and outlet port ("Outlet 1" or "Outlet 2" or 'Waste") and containing a set of microelectrodes ("Trap 2" and page 10, line 22 - page 11, line 09) and a means of moving fluid through the fluidic system (implied by page 07, lines 05-07, which discloses feeding a sample into inlet 2, and also implied by arrows shown in Figure 1, which indicate flowing fluid);

b) applying an AC voltage to the microelectrodes with an appropriate frequency for retaining in the region of the microelectrodes a given type of microparticles which are functionalized with appropriate ligand molecules by positive dielectrophoresis (since Pethig provides microelectrode means for retaining functional microbeads with antibodies, for example, to trap chemical or biochemical species of interest in a fluid flowed over the electrodes, this step is just using the microelectrodes are intended in at least one Pehtig embodiment - page 07, lines 01-17);

c) flowing a suspension of the type of microparticles through the fluidic system and retaining the microparticles at the microelectrodes by means of positive dielectrophoresis (again this step is just another aspect of how Pethig intends to use his apparatus - page 07, lines 01-17);

d) flowing a sample fluid containing the analyte specifically bound by the ligand molecules on the microparticles through the fluidic system, thereby perfusing the

retaining microparticles (again this step is just another aspect of how Pethig intends to use his apparatus – abstract and associated figure and page 07, lines 01-17);

e) detecting the presence of analyte bound to the microparticles (page 07, line 31 – page 08, line 07).

Pethig only appears to mention latex microbeads. See page 07, lines 5-7. However, this is only as an example. As shown by Van Ness polystyrene microbeads and latex microbeads were known alternative support material at the time of the invention so, barring a contrary showing, to substitute polystyrene microbeads for latex ,microbeads is just substitution of one known element for another with predictable results. The microbead composition and size would be chosen based factors such as the nature of the substances to be supported, how the supported substances are to be supported (chemical linking groups or adsorpotion), the amount of substance to be supported, and the ability of the electrical fields to retain large microbeads.

9. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Pethig et al. WO 97/34689 A1 ("Pethig") in view of Pohl US 4,326,934 ("Pohl").

Pethig discloses a fluidic system for analysing biomolecules comprising an inlet port ("Inlet 2" – Figure 1), an outlet port ("Outlet 1" or "Outlet 2" or "Waste"), a set of microelectrodes ("Trap 2" and page 10, lines 22 – page 11, line 09) within a channel connecting the inlet and outlet ports (Fig. 1), means for flowing a fluid through the fluidic system (implied by page 07, lines 05-07, which discloses feeding a sample into Inlet 2, and also implied by arrows shown in Figure 1, which indicate flowing fluid), means for flowing a suspension of a given type of microparticles through the fluidic system (implied by page 07, lines 05-07, which discloses feeding a sample into Inlet 2, and also implied by arrows shown in Figure 1, which indicate flowing fluid), means for applying an AC voltage having an appropriate frequency for retaining a given type of microparticles in the region of the electrodes by means of positive (attractive) dielectrophoresis (implied by page 07, lines 09-10, which states "Trap T2 is of a selective nature and, at this time configured to trap the latex beads."), the microparticles being functionalized with appropriate ligand molecules (page 07, lines 05-07), and means for flowing a sample fluid containing the analyte specifically bound by the ligand molecules on the microparticles through the fluidic system, thereby perfusing the retained microparticles (page 07, lines 22-27, which discloses releasing all trapped particles, including microparticles with analyte bound thereon, and flowing them towards junction JC).

Pethig does not appear to mention how the fluid flow is generated.

Pohl discloses a continuous dielectrophoresis cell classification method in which syringes are used to generate fluid flow through out a dielectrophoresis system. See the title, and Figure 5. In light of Pohl using a syringe to generate fluid flow is just substitution of one known element for another (assuming Pethig uses a different means for generating fluid flow than a syringe) with predictable results.

10. Claims 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pethig et al. WO 97/34689 A1 ("Pethig") in view of Parton et al. WO 93/16383 A1 ("Parton").

Pethig discloses a fluidic system for analysing biomolecules comprising an inlet port ("Inlet 2" – Figure 1), an outlet port ("Outlet 1" or "Outlet 2" or "Waste"), a set of microelectrodes ("Trap 2" and page 10, lines 22 – page 11, line 09) within a channel connecting the inlet and outlet ports (Fig. 1), means for flowing a fluid through the fluidic system (implied by page 07, lines 05-07, which discloses feeding a sample into Inlet 2, and also implied by arrows shown in Figure 1, which indicate flowing fluid), means for flowing a suspension of a given type of microparticles through the fluidic system (implied by page 07, lines 05-07, which discloses feeding a sample into Inlet 2, and also implied by arrows shown in Figure 1, which indicate flowing fluid), means for applying an AC voltage having an appropriate frequency for retaining a given type of

microparticles in the region of the electrodes by means of positive (attractive) dielectrophoresis (implied by page 07, lines 09-10, which states "Trap T2 is of a selective nature and, at this time configured to trap the latex beads."), the microparticles being functionalized with appropriate ligand molecules (page 07, lines 05-07), and means for flowing a sample fluid containing the analyte specifically bound by the ligand molecules on the microparticles through the fluidic system, thereby perfusing the retained microparticles (page 07, lines 22-27, which discloses releasing all trapped particles, including microparticles with analyte bound thereon, and flowing them towards junction JC).

Pethig does not specifically mention whether the detecting means comprises a fluorescence microscope and also having the ligand bound to the microparticles be strepavadin and the analyte contained in the sample be fluorescein labeled biotin. However, Pethig does refer to Patent Application WO93/16382 ("Parton") for more detail on the detection means employed. Parton states, "Preferred marking methods include coating beads or other microparticles with a dye, e.g., a fluorescent dye ... A dye, e.g. a fluorescent dye, may be incorporated as a label into the linking moiety to be attached to the beads or other microparticles." See paged 08, lines 23-35. Also, "The label 36 may be for instance be reactive with an antibody bound to the labeling moiety 32 ... A label may be then be employed comprising an electro-rotation labeling moiety bound to avidin or an avidin like molecule such as strepavidin." See page 16, lines 12-24. Thus, the additional limitations of claims 12 and 13 are fairly disclosed by Pethig through Parton.

11. Claim 40 is rejected under 35 U.S.C. 103(a) as being unpatentable over Pethig et al. WO 97/34689 A1 ("Pethig") in view of Pohl US 4,326,934 ("Pohl") and Parton et al. WO 93/16383 A1 ("Parton").

Pethig discloses a method for analysis of biomolecules comprising the steps of:

a) providing a fluidic system having an inlet port ("Inlet 2" – Figure 1) and outlet port ("Outlet 1" or "Outlet 2" or 'Waste") and containing a set of microelectrodes ("Trap 2" and page 10, line 22 - page 11, line 09) and a means of moving fluid through the fluidic system (implied by page 07, lines 05-07, which discloses feeding a sample into inlet 2, and also implied by arrows shown in Figure 1, which indicate flowing fluid);

b) applying an AC voltage to the microelectrodes with an appropriate frequency for retaining in the region of the microelectrodes a given type of microparticles which are functionalized with appropriate ligand molecules by positive dielectrophoresis (since Pethig provides microelectrode means for retaining functional microbeads with antibodies, for example, to trap chemical or biochemical species of interest in a fluid flowed over the electrodes, this step is just using the microelectrodes are intended in at least one Pehtig embodiment - page 07, lines 01-17);

c) flowing a suspension of the type of microparticles through the fluidic system and retaining the microparticles at the microelectrodes by means of positive dielectrophoresis (again this step is just another aspect of how Pethig intends to use his apparatus - page 07, lines 01-17);

d) flowing a sample fluid containing the analyte specifically bound by the ligand molecules on the microparticles through the fluidic system, thereby perfusing the retaining microparticles (again this step is just another aspect of how Pethig intends to use his apparatus – abstract and associated figure and page 07, lines 01-17);

e) detecting the presence of analyte bound to the microparticles (page 07, line 31 – page 08, line 07).

Pethig does not appear to mention how the fluid flow is generated. Pohl discloses a continuous dielectrophoresis cell classification method in which syringes are used to generate fluid flow through out a dielectrophoresis system. See the title, and Figure 5. In light of Pohl using a syringe to generate fluid flow is just substitution of one known element for another (assuming Pethig uses a different means for generating fluid flow than a syringe) with predictable results.

Pethig does not specifically mention whether the detecting means comprises a fluorescence microscope and also having the ligand bound to the microparticles be strepavadin and the analyte contained in the sample be fluorescein labeled biotin. However, Pethig does refer to Patent Application WO93/16382 ("Parton") for more detail on the detection means employed. Parton states, "Preferred marking methods include coating beads or other microparticles with a dye, e.g., a fluorescent dye ... A dye, e.g. a fluorescent dye, may be incorporated as a label into the linking moiety to be attached to the beads or other microparticles." See paged 08, lines 23-35. Also, "The label 36 may be for instance be reactive with an antibody bound to the labeling moiety 32 ... A label may be then be employed comprising an electro-rotation labeling moiety bound to avidin

or an avidin like molecule such as strepavidin." See page 16, lines 12-24. Thus, the additional limitations of claims 12 and 13 are fairly disclosed by Pethig through Parton.

12. Claims 3, 6, 10, and 16-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gomez et al. US 7,306,924 B2 ('Gomez").

Addressing claim 3, Gomez discloses a fluidic system for analysing biomolecules comprising an inlet port (28 – Figure 1), an outlet port (30), a set of microelectrodes (36) within a channel connecting the inlet and outlet ports (Fig. 1), means for flowing a fluid through the fluidic system (implied by the arrows shown at the inlet port and outlet port. Also see col. 17:50-53 and claim 11, line 3), means for flowing a suspension of a given type of microparticles through the fluidic system (implied by the arrows shown at the inlet port and outlet port. Also see col. 17:50-53 and claim 11, line 3), means for applying an AC voltage having an appropriate frequency for retaining a given type of microparticles in the region of the electrodes by means of positive (attractive) dielectrophoresis (col. 32:11-15 and col. 31:38-41), the microparticles (128) being functionalized with appropriate ligand molecules (col. 32:11 and col. 31:35-37), and means for flowing a sample fluid containing the analyte specifically bound by the ligand

molecules on the microparticles through the fluidic system (col. 32:16-21), thereby perfusing the retained microparticles (col. 32:16-21).

Additionally, as discussed in the rejection of claim 1 Gomez discloses "means for flowing a suspension of a given type of microparticles through the fluidic system (implied by the arrows shown at the inlet port and outlet port. Also see col. 17:50-53 and claim 11, line 3), means for applying an AC voltage having an appropriate frequency for retaining a given type of microparticles in the region of the electrodes by means of positive (attractive) dielectrophoresis (col. 32:11-15 and col. 31:38-41)." Additionally, Gomez states, "The frequency and magnitude of an alternating electric field **158** produced by the electrodes **156**, together with the conductivity of the carrier medium, are chosen so that the microorganisms **160** of interest are retained inside the chamber **154** by the DEP force (in the same way as beads **128** were retained in the previous capture method). [emphasis added]" See col. 32:36-42. The apparatus of Gomez is thus clearly configured with means to flow a mixture of microparticles and substances therein and means to selectively retain microparticles or other substances from the mixture by applying an appropriate frequency to trapping electrodes.

As for providing a plurality of sets of microelectrodes within the channel at spaced intervals, and means for applying voltages of selected frequencies to each of the sets of electrodes to retain selected types of microparticles at the electrodes these features are obvious over Gomez. Providing a plurality of sets of microelectrodes is just multiplication of parts for a multiplied effect (the ability to retain multiple microparticles in different regions of the device), which is *per se* obvious. See MPEP 2144.04.VI.B.

Moreover, Figure 1 in Gomez shows a plurality of cavities (34) along the channel each cavity having its own electrode set (36). This would strongly suggest to one of ordinary skill in the art to provide a plurality of sets of microelectrodes within the channel as claimed.

Addressing claim 6, Gomez discloses a fluidic system for analysing biomolecules comprising an inlet port (28 – Figure 1), an outlet port (30), a set of microelectrodes (36) within a channel connecting the inlet and outlet ports (Fig. 1), means for flowing a fluid through the fluidic system (implied by the arrows shown at the inlet port and outlet port. Also see col. 17:50-53 and claim 11, line 3), means for flowing a suspension of a given type of microparticles through the fluidic system (implied by the arrows shown at the inlet port and outlet port. Also see col. 17:50-53 and claim 11, line 3), means for applying an AC voltage having an appropriate frequency for retaining a given type of microparticles in the region of the electrodes by means of positive (attractive) dielectrophoresis (col. 32:11-15 and col. 31:38-41), the microparticles (128) being functionalized with appropriate ligand molecules (col. 32:11 and col. 31:35-37), and means for flowing a sample fluid containing the analyte specifically bound by the ligand molecules on the microparticles through the fluidic system (col. 32:16-21), thereby perfusing the retained microparticles (col. 32:16-21).

Barring a contrary showing, according to the Examiner's understating of the specification the means for flowing a solution containing reagent molecules specific to the analyte molecules through the fluidic system to perfuse the analyte bound by the ligand molecules on the microparticles can be the same as the means for flowing a suspension of a given type of microparticles through the fluidic system in claim 1 or the means for flowing a fluid through the fluidic system in claim 1.

Gomez does not mention detecting the presence of the reagent molecules bound to the microparticles at the retention site of the microparticles. As a first matter this claim only seems to add an intended use of the system, not an actual structural feature. In any event, since Gomez already discloses reacting anayte with a functional group on the microparticle, to also include additional reagent molecules in the fluid can just be for enchancing detection of the analyte-microparticle complex.

Addressing claims 10 and 39, Gomez discloses using polystyrene beds (col. 31:45-51), although a diameter range does not appear to be also disclosed, barring a contrary showing, such as unexpected results, the diameter of the microbeads will be selected based on the amount of substances to be supported and the ability of the intended electrical fields to retain or otherwise manipulate microbeads with a "large" diameter.

Addressing claim 16, Gomez discloses a method for analysis of biomolecules comprising the steps of:

a) providing a fluidic system having an inlet port (28 – Figure 1) and outlet port (30) and containing a set of microelectrodes (36) and a means of moving fluid through the fluidic system (implied by arrows shown at the inlet port and outlet port. Also see col. 17:50-53 and claim 11, line 3);

b) applying an AC voltage to the microelectrodes with an appropriate frequency for retaining in the region of the microelectrodes a given type of microparticles which are functionalized with appropriate ligand molecules by positive dielectrophoresis (since Gomez provides microelectrode means for retaining functional microbeads with antibodies, for example, to trap chemical or biochemical species of interest in a fluid flowed over the electrodes, this step is just using the microelectrodes are intended in at least one Gomez embodiment – col. 32:11-29 and col. 31:38-41);

c) flowing a suspension of the type of microparticles through the fluidic system and retaining the microparticles at the microelectrodes by means of positive dielectrophoresis (again this step is just another aspect of how Gomez intends to use his apparatus – col. 32:11-29);

d) flowing a sample fluid containing the analyte specifically bound by the ligand molecules on the microparticles through the fluidic system, thereby perfusing the retaining microparticles (again this step is just another aspect of how Gomez intends to use his apparatus – col. 32:16-21);

e) detecting the presence of analyte bound to the microparticles (implied since the retaining chamber also functions as a detection chamber – col. 32:11-15).

Addressing claim 17, Gomez discloses "means for flowing a suspension of a given type of microparticles through the fluidic system (implied by the arrows shown at the inlet port and outlet port. Also see col. 17:50-53 and claim 11, line 3), means for applying an AC voltage having an appropriate frequency for retaining a given type of microparticles in the region of the electrodes by means of positive (attractive) dielectrophoresis (col. 32:11-15 and col. 31:38-41)." Additionally, Gomez states, "The frequency and magnitude of an alternating electric field **158** produced by the electrodes **156**, together with the conductivity of the carrier medium, are chosen so that the microorganisms **160** of interest are retained inside the chamber **154** by the DEP force (in the same way as beads **128** were retained in the previous capture method). [emphasis added]" See col. 32:36-42. The apparatus of Gomez is thus clearly configured with means to flow a mixture of microparticles and substances therein and means to selectively retain microparticles or other substances from the mixture by applying an appropriate frequency to trapping electrodes.

Addressing claim 18, detecting the presence of the analyte bound to the micro particles at the retention site of the microparticles is implied in Gomez because the cavities containing the retention sites as detection/collection chambers. See col. 32:11-15. Also see co. 30:31-56.

Addressing claims 19, 20, and 22-24, barring a contrary showing, according to the Examiner's understating of the specification the means for flowing a solution containing reagent molecules specific to the analyte molecules through the fluidic system to perfuse the analyte bound by the ligand molecules on the microparticles can be the same as the means for flowing a suspension of a given type of microparticles through the fluidic system in claim 16 or the means for flowing a fluid through the fluidic system in claim 16.

Gomez does not mention detecting the presence of the reagent molecules bound to the microparticles at the retention site of the microparticles. Since Gomez already discloses reacting anayte with a functional group on the microparticle, to also include

additional reagent molecules in the fluid can just be for enchancing detection of the analyte-microparticle complex. Note that if the reagent is to enhance or enable detection of the analyte then when the reagent is detected the analyte, at least indirectly, will also be detected and vice verse. In any event, the apparatus of Gomez can clearly detect reagent or analyte as desired, since they are chemical or biochemical species. Also note that using a washing fluid and the sequence in which washing fluid and reagent is flowed is within the skill of one ordinary skill in the art at the time of the invention knowing the reaction involved between the reagent and analyte or microparticle to determine how to implement the reagent reaction and wash off excess reagent or unwanted chemical byproducts.

Addressing claim 21, for the additional limitation of this claim see col. 32:21-27.

Addressing claims 25-35, the additional limitations of these claims concern how long the AC field is applied, whether reagent is used and when during the analyte process, and whether, when rinsing is performed, and whether detection occurs in the regain region or outside of it. If not already taught by Gomez these steps are within the skill of one of ordinary sill in the art at the time of the invention as they are just optimizing the detection process. For example how long the microparticles are retained

just depends on the whether the analyte-ligand reaction or analyte-reagent reactions have occurred to the extent desired (amount or volume of sample to evaluated and kinetics of the reactions) and whether detection will occur at the retaining site or not. Gomez does not mention detecting the presence of the reagent molecules bound to the microparticles at the retention site of the microparticles. Since Gomez already discloses reacting analyte with a functional group on the microparticle, to also include additional reagent molecules in the fluid can just be for enhancing detection of the analyte-microparticle complex. Note that if the reagent is to enhance or enable detection of the analyte then when the reagent is detected the analyte, at least indirectly, will also be detected and vice verse. In any event, the apparatus of Gomez can clearly detect reagent or analyte as desired, since they are chemical or biochemical species. Also note that using a washing fluid and the sequence in which washing fluid and reagent is flowed is within the skill of one ordinary skill in the art at the time of the invention knowing the reaction involved between the reagent and analyte or microparticle to determine how to implement the reagent reaction and wash off excess reagent or unwanted chemical byproducts.

Addressing claim 36, for the additional limitations of this claim see col. 13:50 - col. 14:40.

Addressing claim 37, for the additional limitations of this claim see col. 28:40-44.

Addressing claim 38, the relative size of the microelectrodes to the fluid channel width and the dimensions of the microelectrodes, such as width and gap spacing will just depend on the expected size of the microparticles, and the electrical field to be generated.

13. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gomez et al. US 7,306,924 B2 ('Gomez") in view of Pohl US 4,326,934 ("Pohl").

Addressing claim 1, Gomez discloses a fluidic system for analysing biomolecules comprising an inlet port (28 – Figure 1), an outlet port (30), a set of microelectrodes (36) within a channel connecting the inlet and outlet ports (Fig. 1), means for flowing a fluid through the fluidic system (implied by the arrows shown at the inlet port and outlet port. Also see col. 17:50-53 and claim 11, line 3), means for flowing a suspension of a given type of microparticles through the fluidic system (implied by the arrows shown at the inlet port and outlet port. Also see col. 17:50-53 and claim 11, line 3), means for applying an AC voltage having an appropriate frequency for retaining a given type of microparticles in the region of the electrodes by means of positive (attractive) dielectrophoresis (col. 32:11-15 and col. 31:38-41), the microparticles (128) being

functionalized with appropriate ligand molecules (col. 32:11 and col. 31:35-37), and means for flowing a sample fluid containing the analyte specifically bound by the ligand molecules on the microparticles through the fluidic system (col. 32:16-21), thereby perfusing the retained microparticles (col. 32:16-21).

Gomez does not appear to mention how the fluid flow is generated.

Pohl discloses a continuous dielectrophoresis cell classification method in which syringes are used to generate fluid flow through out a dielectrophoresis system. See the title, and Figure 5. In light of Pohl using a syringe to generate fluid flow is just substitution of one known element for another (assuming Gomez uses a different means for generating fluid flow than a syringe) with predictable results.

Claim Rejections - 35 USC § 112

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claim 16 recites the limitation "said electrodes" in lines 6 and 8. There is insufficient antecedent basis for this limitation in the claim.

International Search Report for International Application No. PCT/EP03/10206

('Search Report")

16. DE 19903001A has been cited as an "X" reference in the Search Report against claims 1, 2, 4, 14, 16-18, and 26. Claim 1 requires "... means for applying an AC voltage having an appropriate frequency for retaining a given type of microparticles in the region of the electrodes by means of positive (attractive) dielectrophoresis, the microparticles begin functionalised with appropriate ligand molecules, ..." US Patent No. 6,801,311 B1 ("Fuhr") is an English language equivalent of DE 19903001A.

Figure 15 in Fuhr shows an embodiment in which ligand molecules are retained in the region of the electrodes. However, the ligand molecules are not functionalized on microparticles nor are they retained by an AC voltage applied to the electrodes. There is no mention of how the ligand molecules are retained (col. 10:29-34), presumably they are retained by conventional chemical bonding means to the channel floor. The passages cited by the European Examiner in the Search Report only disclose using AC fields to manipulate biological cells in the corresponding passages in Fuhr.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALEX NOGUEROLA whose telephone number is (571) 272-1343. The examiner can normally be reached on M-F 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, NAM NGUYEN can be reached on (571) 272-1342. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Alex Noguerola/
Primary Examiner, Art Unit 1795
May 25, 2009